REMARKS

Applicants note that all amendments and cancellation of Claim herein are made in order to further their business interests and the prosecution of the present application, yet without acquiescing to the Examiner's arguments, and while preserving the right to prosecute the canceled (or similar) claims in the future.

I. The Claims are Definite

The Examiner rejects Claims 12, 15 and 17-20 under 35 U.S.C. 112, second paragraph as allegedly indefinite. In particular, the Examiner states "The metes and bounds of the limitation are unclear because table 1…only recites number identifiers, molecular weights and isolectric points." (Office Action, pg. 3) Applicants respectfully disagree. Nonetheless, in order to further the business interests of the Applicants, and without acquiescing to any of the Examiner's arguments or rejections, and solely for the purpose of expediting the patent application process in a manner consistent with the PTO's Patent Business Goals (PBG), and without waiving the right to prosecute the cancelled claims (or similar claims) in the future, the Applicants have amended Claim 12. Amended Claim 12 recites that the proteins are identified by molecular weight and isoelectric point. Applicants submit that the proteins are made definite by their molecular weights and isolectric points and their specificity to breast cancer, as described in the specification. Accordingly, applicants submit that the claims are definite and respectfully request that the rejection be withdrawn.

II. The Claims are Not Obvious

The Examiner rejects Claims 12 and 18 under 35 U.S.C. 103(a) as allegedly obvious in light of Miyagi et al. (US 4,338,811; hereinafter Miyagi) in view of Sidransky (Nature Reviews 2002 2:210; hereinafter Sidransky) as supported by Romero et al. (Eur. Respir. J. 1996 9:17; hereinafter Romero). The Examiner further rejects Claims 12, 15 and 17-18 under 35 U.C.C. 103(a) as allegedly obvious in light of Miyagi in view of Sidransky as supported by Romero and further in view of Srinivas et al. (Clinical Chemistry 2001 47:1901; hereinafter Srivivas). The Examiner additionally rejects Claims 12 and 18-20 under 35 U.S.C. 103(a) as allegedly obvious in light of Miyagi in view of Sidransky as supported by Romero and further in view of

Vachtesvanos et al. (US 6,650,779; hereinafter Vachtesvanos) and Karlsen et al. (Opt. Eng. 2000 39:704; hereinafter Karlsen).

Applicants respectfully disagree. Nonetheless, in order to further the business interests of the Applicants, and without acquiescing to any of the Examiner's arguments or rejections, and solely for the purpose of expediting the patent application process in a manner consistent with the PTO's Patent Business Goals (PBG), and without waiving the right to prosecute the cancelled claims (or similar claims) in the future, the Applicants have amended Claim 12. Amended Claim 12 specifies that the proteome standard is generated by the methods described in Claims 19-20. Claims 19-20 have been canceled.

Applicants note that the rejections under Miyagi in view of Sidransky and Romero and Miyagi in view of Sidransky, Romero and Srinivas are moot as Claims 19-20 were not included in these rejections. Neither Miyagi, Sidransky, Romero nor Srinivas, alone or in combination, teach the elements of amended Claim 12 of an image preprocessing step classification step with a genetic algorithm or fidelity estimation using a SVM. Nor do the cited references teach the step of fuzzy data mapping, quantifying statistical inaccuracy using a fuzzy technique and a rule-based classification step (Office Action, pg. 9).

Applicants address the rejection under Miyagi in view of Sidransky, Romero, Srinivas, Vachtesvanos and Karlsen below. The Examiner states

> "It would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the methods of disease diagnosis of Miyagi et al in view of Sidransky with the image pre-processing and feature classification by Vachtesvanos et al and the classification SVM algorithm by Karlsen et al. because Vachtesvanos et al. shows that image pre-processing enhances the real signal and improves the quality of feature extraction while the multidimensional neural network analyzes and identifies patterns efficiently and economically while lessening the need for human assistance…and Karlsen et al. shows that the SVM algorithm give higher correct classification results compared to neural networks." (Office Action, pg. 10).

Applicants respectfully disagree and submit that the Examiner has not demonstrated a prima facie case of obviousness as required under 35 U.S.C. 103 because the cited references do not provide a motivation to combine the cited references with a reasonable expectation of success.

For example, in contrast to the presently claimed invention, in which the spots used as diagnosis marker of breast cancer are described by their molecular weights and isolectric points,

Sidransky and Romero describe markers only by molecular weight. In addition, Sidransky and Romero disclose only 7 markers, none of which have molecular weights that correspond to the molecular weights described in Table 1. Neither Sidransky nor Romero discloses the use of isoelectric points to further define the proteins used as standards. This is in direct contrast to the methods of the presently claimed invention, which identify proteins by both molecular weight and isoelectric points. Miyagi utilizes chromatography data and is silent on the use of molecular weight and isoelectric point in the generation of proteomic maps.

Furthermore, neither Vachtesvanos nor Karlsen, alone or in combination, teach that pre-processing a digitized 2D image using a genetic algorithm, estimation functions, classification error rates, fuzzy data mapping, fuzzy rule-base classification or SVM is useful in generating a serum proteome standard. Vachtesvanos and Karlsen are silent on the use of the disclosed methods to analyze proteome standards with protein molecular weight and isoelectric point data. Indeed, Vachtesvanos and Karslen are unrelated to the biological sciences and thus would not have reasonably been considered by one working in the field of proteomics. Thus, one of skill in the art would not have been motivated to use the techniques described in Vachtesvanos or Karlsen in combination with the methods of Miyagi because Vachtesvanos and Karlsen are in non-analogous areas of art and neither teach nor suggest the analysis of proteomic data.

In addition, since Miyagi does not teach or suggest the use of proteomes identified by molecular weight and isoelectric point and Sidransky and Romero do not teach the use of isolectric point in further defining proteomes, and Vachtesvanos and Karlsen are not related to proteomic analysis, absent the present invention, one of skill in the art would not have expected the combination of the cited references to result in the methods of the presently claimed invention. Absent the present invention, one of ordinary skill in the art would not have been able to have a reasonable expectation of success that the techniques of Vachtesvanos and Karlsen would be successful in analyzing proteomics data to generate 2D images that are suitable for diagnosing breast cancer. The Examiner has pointed to no teaching in any of the cited references that the combination of references provides an expectation of success that the combination would successfully result in the presently claimed invention.

Applicants further note that Claims 12 and 18 of the presently claimed invention specify that ability to discriminate spots having optimal features playing a critical role in classification of disease-specific spots by genetic algorithm and estimate fidelity of the optimal feature data by

SVM. Also, the claims specify the use of a fuzzy rule-based classification step to improve specification and recognition accuracy. Absent the present invention, one of ordinary skill in art would not have had a reasonable expectation of success that the combination of references cited by the examiner would result in such improvements.

In addition, none of the cited references render obvious the method of claim 15 of evaluating the progression status and future prognosis of disease by statistical and experimental methods as well as detection of cancer or the method of Claim 17 of classification into categories of normal or having a disease by the pattern matching. Absent the present invention, one of ordinary skill in art would not have had a reasonable expectation of success that the combination of references cited by the examiner would result in the presently claimed invention. Nor has the Examiner pointed to any evidence, in the cited references or otherwise, that provides such an expectation.

Applicants submit that the Examiner has not demonstrated a prima facie case of obviousness because the cited references do not provide a motivation to combine the references with a reasonable expectation of success.

CONCLUSION

If a telephone interview would aid in the prosecution of this application, the Examiner is encouraged to call the undersigned collect at (608) 662-1277

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